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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,347	03/04/2002	Peter H. Tang		3959

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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	
ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,347	TANG ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) *1-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03042002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. Claims 1 and 10 are objected to because of the following informality: -- and -- should be inserted at the end of lines 6 and 5, respectively.

2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. Claims 2-9 and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a) Claim 2 does not further structurally limit claim 1 because claim 2 only provides for intended treatment of an unclaimed sample. As stated, claim 2 does not require a chromatographic column in the apparatus;

b) Claim 3 does not further structurally limit claim 2 because claim 3 only provides for intended voltage to be applied to the coulometric guard cell;

c) Claim 4 does not further structurally limit claim 3 because claim 4 only provides for intended voltages to be applied to the electrodes in the analytical cell;

c) The statutory class of invention for claims 2-4 is indefinite as claim 1 is directed to an apparatus, but claims 2-4 appear to only provide method steps for using the apparatus of claim 1;

d) Claims 5-9 do not further structurally limit the claims from which they depend because these claims only limit a sample solution that is not part of the apparatus; that is, which is only intended use; and

e) Claim 13 recites the limitation "said aqueous sample solution" in line 1. There is insufficient antecedent basis for this limitation in the claim.

4. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Matson (US 4,552,013), hereafter "Matson."

Addressing claims 1-9, Matson teaches an apparatus for electrochemically analyzing an aqueous sample solution (abstract) comprising electrochemically reversible materials in solution, the apparatus comprising

a) a coulometric guard cell (23), the coulometric guard cell arranged in series with an analytical cell (36) which is downstream from the guard cell (Figures 1, 5, and 6), the guard cell and the analytical cell being arranged so as to define collectively at least one flow channel for the sample solution (Figures 1, 5, and 6);

b) the analytical cell consisting essentially of a series of at least two coulometric electrodes (col. 7, ll. 38-41)[1].

Matson does not mention *operating* the coulometric guard cell in an oxidative mode

[1] The Model No. 5010 electrochemical detection cell from E.S.A., Inc. has two coulometric electrodes in series. See "Electrochemical Cell Designs for Coulochem® for Coulochem Detectors," downloaded from the ESA Inc. web site.

However, this limitation is only intended use that does not further structurally limit the coulometric guard cell. Matson teaches, for example, applying a voltage of –0.50 V in the guard cell (col. 7, ll. 43-46), which may or may not be oxidative depending on the sample.

Matson also does not mention operating the analytical cell so that the first electrode *operates* in a reductive mode and the second electrode *operates* in an oxidative mode at a potential which simultaneously detects and coulometrically measures electrochemically reversible materials in the sample solution. However, this limitation is only intended use that does not further structurally limit the analytical cell. Whether an electrode is operating oxidatively or reductively depends on the voltage of the electrode and the species undergoing electron transfer with the electrode.

For claims 2-9, note that these claims does not further structurally limit the apparatus of the claims from which they immediately depend (see the rejections of claims 2-9 under 35 U.S.C. 112, second paragraph, above).

Addressing claim 10, Matson teaches a method for simultaneously analyzing a mixture of electrochemically reversible materials comprising the steps of

a) passing the materials through a liquid chromatographic column for achieving time-spaced separation of the materials from the column (Figure 1 and col. 7, ll. 27-38)[2];

a) oxidizing the materials by passing the materials through a coulometric guard cell

[2] "'Unless the steps of a method actually recite an order, the steps are not ordinarily construed to require one. However, such a result can ensue when the method steps implicitly require that they be performed in the order written. In this case, nothing in the claim or the specification directly or implicitly requires such a narrow construction.'" *Interactive Gift Express, Inc. v. Compuserve Inc.* 59 USPQ2d 1401, 1416 (citations omitted).

(abstract; Figure 1; and col. 7, ll. 16-26);

b) passing the materials through an analytical cell consisting essentially of a series of at least two coulometric electrodes (col. 7, ll. 38-41)[3];

the at least two coulometric electrodes being arranged in series and defining collectively at least one flow channel for the sample solution (col. 7, ll. 38-41)[4].

Addressing claims 11 and 12, Matson does not mention the claimed voltages for the coulometric guard cell and the electrodes in the analytical cell; however, barring evidence to the contrary, such as unexpected results, especially since the sample has not been specified, the voltages used are just a matter of optimizing the apparatus within the skill of one with ordinary skill in the art at the time of the invention. The voltage in the coulometric guard cell will depend on the background material to be removed (col. 6, ll. 47-62) and voltages for the electrodes in the analytical cell will depend on the analyte(s) to be detected.

7. Claims 1-17 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Tang et al. ("HPLC Analysis of Reduced and Oxidized Coenzyme Q_{10} in Human Plasma," *Clinical Chemistry* 47:2, 258-265 (February 01, 2001), hereafter "Tang I."

For the claim limitations see Figure 1, "Apparatus" on page 257 bridging to page 258,

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[3] ESA Inc., ibid.

[4] Ibid.

and "Coulometric Detection" on page 258 bridging to page 259.

For claims 2-4, note that these claims does not further structurally limit the apparatus of claims from which they immediately depend (see the rejections of claims 2-4 under 35 U.S.C. 112, second paragraph, above). In any event, as regards claims 3 and 4, the claimed voltages are taught ("Coulometric Detection" on page 258), and, as regards claims 5-9, CoQ_{10}, $CoQ10H_{2}$,, human plasma, and 1-propanol are taught ("Preparation of Calibrators" and "Preparation of Plasma samples" on page 258).

For claim 10 note that the order of the steps is not specified, so step (a) may occur after step (b) and before step (c)[5].

For claims 11 and 12 note that the claimed voltages are taught ("Coulometric Detection" on page 258).

For claims 13-17 note that CoQ_{10}, $CoQ10H_{2}$,, human plasma, and 1-propanol are taught ("Preparation of Calibrators" and "Preparation of Plasma samples" on page 258).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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[5] *Interactive Gift Express, Inc, ibid.*

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. ("Simple and rapid HPLC method with coulometric detection of coenzyme Q10 in human plasma and CSF," *Book of Abstracts*, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000), hereafter "Tang II," in view of Schieffer ("Precolumn Coulometric Cell for High-Performance Liquid Chromatography," *Anal. Chem.* 1981, 63, 126-127), hereafter "Schieffer."

Tang II teaches an apparatus for electrochemically analyzing an aqueous sample solution (abstract) comprising electrochemically reversible materials in solution, the apparatus comprising

a) an electrochemical cell arranged in series with an analytical cell which is downstream from the electrochemical cell (abstract), the electrochemical cell and the analytical cell being arranged so as to define collectively at least one flow channel for the sample solution (implied by the abstract, which teaches that the electrochemical cell is located before an HPLC column and the analytical cell is located after the HPLC column;

b) the analytical cell consisting of two electrodes operated in reduction-oxidation mode at a potential which measures materials in the sample (abstract).

Tang II does not mention whether the electrochemical cell is a coulometric cell. It should be noted that labeling an electrochemical cell as a coulometric cell is arguably just intended use that does not necessarily structurally limit the electrochemical cell, unless it had a meter configured for coulometric measurement, for example. An amperometric cell could also be used for coulometry since coulometry is a similar measurement *method*. Assuming, though, that "coulometric" in coulometric cell is structurally limiting, as seen from Schieffer, it was known at the time of the invention to use a coulometric cell before a chromatography column (Figure 1 of Schieffer). It would have been obvious to one with ordinary skill in the art at the time the invention was made to use a precolumn coulometric cell as taught by Schieffer in the invention of Tang II because as taught by Schieffer will yield 100% electrolysis (second

paragraph in the first column on page 126), which is desirable in Tang II as the electrochemical cell is for converting CoQ10 into reduced CoQ10.

Tang II also does not mention whether the electrodes for reduction-oxidation in the analytical cell are coulometric electrodes; however, the intended use of these electrodes does not structurally limit them, barring a contrary showing.

For claims 2-9, note that these claims does not further structurally limit the apparatus of claims from which they immediately depend (see the rejections of claims 2-4 under 35 U.S.C. 112, second paragraph, above). In any event, as regards claims 5-9, CoQ_{10}, human plasma, and 1-propanol are taught and $CoQ10H_2$ is implied by Tang II.

For claim 10 note that abstract states or implies passing materials from a sample through the apparatus discussed above and the order of the steps is not specified, so step (a) may occur after step (b) and before step (c)[6].

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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[6] Ibid.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753
May 27, 2004